Amendments to the Specification

Please replace the paragraph beginning on Page 1, line 7 with the following paragraph.

> The picornavirus family encompasses single-stranded positive-sense RNA viruses, encapsulated in a protein capsid (Reviewed in Rucekert, 1996, in Fields, Virology, 609-654). These viruses cause a wide range of diseases in humans and other mammals, including the common cold (rhinoviruses), gastro-intestinal ailments (enteroviruses, such as coxsackievirus and echovirus), poliomyelitis (the enterovirus poliovirus), heart diseases (cardioviruses), hepatitis (hepatitis A) and foot and mouth disease (aphtoviruses). Rhinoviral common cold is of specifically noted medical and economical significance, due both to its ubiquity (the major cause of acute illness in the ~~united states~~ United States) and to ~~thee~~ the debilitating effect of the disease and consequential loss of work days (see McKinlay, *Ann. Rev. Microbiol.*, **46**:635-54, 1992). Related viral families of the picornavirus supergroup, such as flaviviridae and potyviridae, cause various diseases in agriculturally significant crops, such as potatoes (see Ryan, J. Gen Virol., **4**:699-723, 1997).

Please replace the paragraph beginning on Page 6, line 1 with the following paragraph.

> Examples of specific compounds according to the present invention are compounds of the following formulae II - ~~XIX~~ XVII, it being noted that these compounds are all specific examples of compounds of formula I:

Please replace the paragraph beginning on Page 14, line 12 with the following paragraph.

> Alternatively, R_1 is an oligopeptide of 1 to 5 amino acid units capable of specifically recognizing and binding to the active site of the species-specific 3C protease against which the inhibitor is directed, since the active site of each 3C protease differs slightly ~~form~~ from one type of picornavirus to the other. Generally speaking, the oligopeptide should be able to mimic the amino acid sequence of the viral proteins to which the 3C protease binds; some of these amino acids are conserved and common to all picornaviruses, while others vary between the sub-families, and species. This description is true for all oligopeptides disclosed as substituents herein.

Please replace the paragraph beginning on Page 20, line 13 with the following paragraph.

2,4-dihydroxy-6-methoxyhexanophenone (cf. compound 108; 10 mg, 0.04 mmol) was reacted with sulfuryl chloride in a manner analogous to that described in compound 15 above. The product was ~~vaccuum-dried~~ vacuum-dried, resulting in orange crystals (12 mg). ^{1}H NMR ($CDCl_3$) : δ 14.02 (s, 1H), 6.51 (s, 2H) (s, 1H), 3.91 (s, 3H), 3.05 (t, 2H), 1.69 (t, 2H), 1.32 (m, 4H), 0.89 (t, 3H).

Please replace the paragraph beginning on Page 22, line 3 with the following paragraph.

Dihydroxyanisole (0.500 g, 3.57 mmol), zinc chloride (170 mg) and acetonitrile (0.214 ml, 4.10 mmol) in 35 ml of dry ether were stirred at room temperature. A steady stream of dry gaseous hydrogen chloride was passed through the mixture, and after 10 minutes, the solution turned cloudy and a brown oil separated. In the course of another 5 minutes, the solution above the oil cleared. After 2.5 hours, 25 ml cold water were added, and the mixture was left overnight. The aqueous phase was extracted with water and concentrated by ~~bioling~~ boiling on a hot-plate. Pink crystals began to form after the volume of the aqueous phase was reduced by half, and accumulated on cooling, resulting in 94 mg, 68 mg of which were recrystallized in water to yield 34 mg of pink cyrstals, M.P. 201-202°C. TLC (dichloromethane:ether 7:3), $R_f = 0.57$. UV, $\lambda = 287.3$nm (εmM=18.5cm^{-1}M^{-1}). ^{1}H NMR ($CDCl_3$, 200 MHz) : δ 12.0 (s, 1H; chelated) [DMSO-d_6: δ 13.82 (s, 1H; chelated)], 7.38 (s, 1H, broad) [DMSO-d_6: δ 9.2-11.8 (s, 1H; broad)], 5.96 (s, 1H), 5.65 (s, 1H), 3.87 (s, 3H), 2.61 (s, 3H).

Please replace the paragraph beginning on Page 26, line 11 with the following paragraph.

Substrate: Peptide of sequence [(N-Ac)Arg-Ala-Glu-Leu-Gln-Gly-Pro-Tyr-Asp-Glu-NH_2], representing the consensus sequence for cleavage by HRV-3C, was obtained from Peptide Core ~~Faclility~~ Facility (Queen's University, Ontario). Stock solutions of 10 mg/ml were prepared in 100 mM Tris-HCl (pH 8.0).

Please replace the paragraph beginning on Page 28, line 3 with the following paragraph.

The specificity of DIF1 as an enzyme inhibitor was tested using cleavage assays for a number of other enzymes, including elastase, cathepsin B, chymotripsin, papain and ficin A. Elastase was particularly important because it is present in red blood cells, so

that inhibition of its activity could potentially be highly toxic. The results showed that DIF1 does not ~~non-specific inhibition of other~~ specifically inhibit the activity of other enzymes. The experimental method was as follows.

Please replace the paragraph beginning on Page 29, line 19 with the following paragraph.

H1-HeLa cells, obtained from ATCC (F-13824, 1958-CRL) were cultured in MEM (Minimum Essential Medium) supplemented with 10% heat-inactivated fetal calf serum (FCS) by incubation at 37° C, 5% ~~CO2~~ CO_2 (Biological Industry, Kibbuts Beit HaEmek, Israel).

Please replace the paragraph beginning on Page 29, line 22 with the following paragraph.

96 well plates were seeded to 90% confluency. After 12-24 hrs of incubation, the cell's monolayer was ~~wased~~ washed with phosphate-buffered saline (PBS), and the cells were subsequently infected with ten-fold dilutions in PBS (log10) of human rhinovirus 14, strain 1059, obtained from ATCC.

Please replace the paragraph beginning on Page 29, line 26 with the following paragraph.

For each concentration of compound, three rows of wells containing various dilutions of virus were used. After 1 h of incubation at room ~~temperatura~~ temperature, medium containing 3% FCS and various concentrations of compound to be tested was placed in the well. After 2 days incubation at 34° C, 5% ~~CO2~~ CO_2, the cells were fixed by 10% formaldehyde and stained with methylene blue to determine cell viability. The cytopathic effect of non-viable cells was arbitrarily set to 100% for the untreated viral infection, so that the effect of each compound on cell viability was determined according to this baseline. Each experiment was performed 5 times for each compound, and the inhibition of cytopathic effect (ICE_{50}) for inhibition of viral activity was calculated. Compounds were tested at concentrations lower than 50% toxic dose (TD_{50}) previously found. ICE_{50} refers to the concentration in which 50% of the cells remain viable after viral infection.

Please replace the paragraph beginning on Page 33, line 7 with the following paragraph.

Alternatively, the compounds of the invention may be encapsulated, tableted or prepared in an emulsion or syrup for oral administration. Pharmaceutically acceptable

solid or liquid carriers may be added to enhance or stabilize the composition, or to facilitate preparation of the composition. Liquid carriers include syrup, soy bean oil, peanut oil, olive oil, glycerin, saline, ethanol, and water. ~~Solubizing~~ Solubilizing agents, such as dimethylsulfoxide, ethanol or formamide, may also be added. Carriers, such as oils, optionally with ~~solubizing~~ solubilizing excipients, are especially suitable. Oils include any natural or synthetic non-ionic water-immiscible liquid, or low melting solid, which is capable of dissolving lipophilic compounds. Natural oils, such as triglycerides are representative~~,~~. In fact, another aspect of this invention is a pharmaceutical composition comprising a compound of formula (I) and an oil.